Brush cytology in the assessment of pancreatico–biliary strictures: a review of 406 cases

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Abstract

Aims—To assess the accuracy of brush cytology in patients investigated for pancreatico–biliary strictures.

Methods—All pancreatico–biliary brush cytology specimens submitted from two major teaching hospitals over a 6.5 year period were reviewed. Four hundred and forty eight satisfactory specimens from 406 patients with adequate clinical and/or pathological follow up data were examined in the study period.

Results—Two hundred and forty six patients (60.6%) were shown to have neoplastic strictures. One hundred and forty seven tumours were identified cytologically, including 87 of 146 pancreatic carcinomas, 29 of 47 cholangiocarcinomas, one of one bile duct adenoma, four of seven carcinomas of the gallbladder, eight of 13 ampullary carcinomas, two of three ampullary adenomas, 10 of 16 malignancies of undetermined origin, none of two islet cell tumours, one of three hepatocellular carcinomas, and five of eight metastatic tumours. The three adenomas identified on brush cytology could not be distinguished from adenocarcinoma morphologically. One hundred and sixty patients (39.4%) had benign strictures, most often as a result of chronic pancreatitis and bile duct stones. There were three false positive cytological diagnoses mainly as a result of the misinterpretation of cases with relatively scant and/or degenerative atypical epithelial cells. Forty one cases were reported as atypical or suspicious of malignancy on brush cytology, of which 29 were ultimately shown to have carcinoma. The overall diagnostic sensitivity and specificity were 59.8% and 98.1%, respectively. The sensitivity increased from 44.3% in the initial third of cases to 70.7% in the final third of cases examined in the series.

Conclusions—Brush cytology, in conjunction with other clinical and radiological investigations, is a useful technique in the assessment of patients with suspected pancreatico–biliary neoplasia.

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Keywords: brush cytology; pancreatico–biliary strictures; pancreatico–biliary neoplasia

Biliary and pancreatic duct strictures are most often caused by inflammatory or neoplastic disorders involving the pancreas, biliary tree, gallbladder, or ampulla. Conservative management with endoscopic stenting is used in most benign strictures, and also in many patients with malignant tumours, most of whom have locally advanced disease or distant metastases at presentation, precluding the possibility of curative resection. In such cases, an accurate tissue diagnosis, preferably obtained without the need for laparotomy, helps to plan further management, particularly if patients with neoplasia are to be included in therapeutic clinical trials. Conversely, surgical intervention might be appropriate in some patients with apparently localised disease, regardless of the cause of the stricture, and also for symptomatic relief in patients with irresectable tumours and complications caused by local spread. Although preoperative histological or cytological confirmation of neoplasia is less crucial in these cases, ideally a tissue diagnosis should be obtained whenever possible.

Biliary and pancreatic duct lesions are not always readily accessible to biopsy, and cytological techniques have become the initial diagnostic modality in many cases. In general, the examination of bile, and of pancreatic or duodenal fluid aspirates, has been disappointing because cellular preservation is often poor, relatively few malignancies are identified, and occasional false positive results have been described. Percutaneous radiologically guided fine needle aspiration (FNA) is a very accurate technique, particularly in the diagnosis of pancreatic cancer, but is operator dependent and requires a sufficiently distinct mass lesion for targeting. Concerns have also been raised regarding potential tumour spread after percutaneous pancreatic biopsy, although data are conflicting. Brush cytology performed at endoscopic retrograde cholangiopancreatography (ERCP) has now become the preferred initial method of pursuing tissue diagnosis in many patients with pancreatico–biliary strictures. The technique has a low complication rate and allows sampling from most sites within the pancreatic and biliary duct systems. Brushing specimens usually yield well preserved, cellular samples suitable for cytological analysis as indicated by the low unsatisfactory rate (around 5%) in most studies.

The diagnostic specificity of biliary brush cytology is very high and few false positive diagnoses have been reported. The major limitation of the technique has been the relatively modest diagnostic sensitivity recorded in most studies to date. Kurzawinski and colleagues
Table 1  Correlation between cytological diagnosis and the final clinicopathological diagnosis for the 406 patients

<table>
<thead>
<tr>
<th>Clinicopathological diagnosis</th>
<th>Cytological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Benign (n = 160)</td>
<td>145</td>
</tr>
<tr>
<td>Neoplastic (n = 246)</td>
<td></td>
</tr>
<tr>
<td>Carcinoma of pancreas (n = 146)</td>
<td>40</td>
</tr>
<tr>
<td>Cholangiocarcinoma (n = 48)</td>
<td>12</td>
</tr>
<tr>
<td>Ampullary neoplasm (n = 16)</td>
<td>6</td>
</tr>
<tr>
<td>Gallbladder carcinoma (n = 7)</td>
<td>2</td>
</tr>
<tr>
<td>Malignant, site ND (n = 16)</td>
<td>3</td>
</tr>
<tr>
<td>Islet cell tumour (n = 2)</td>
<td>2</td>
</tr>
<tr>
<td>HCC (n = 3)</td>
<td>2</td>
</tr>
<tr>
<td>Metastasis (n = 8)</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>215</td>
</tr>
</tbody>
</table>

The ampullary neoplasm category included three adenomas of ampulla and the cholangiocarcinoma group included one bile duct adenoma. HCC, hepatocellular carcinoma; ND, not determined.

reviewed six early series, comprising between nine and 65 patients, and found the mean sensitivity to be 59% (range 54–66%). Similarly, Fouché documented a mean sensitivity of 59% in an analysis of 10 studies, comprising between 19 and 72 patients, although the range was wider (42–85%) in these reports. More recently, five large studies of brush cytology have recorded sensitivities of only 35–48% in patients with pancreatico–biliary malignancy.9–13 However, not all the data are comparable. Some studies have examined only pancreatic duct14–16 or bile duct strictures,17 although most have included a variable proportion of ampullary, biliary, and pancreatic duct lesions. Equally, there is inconsistency in the range and assessment of cytological diagnoses. Although some reports describe only definite positive or negative findings, many authors have included an indeterminate diagnostic category variably classified as atypical, dysplastic, or suspicious of malignancy.9,10,18–20

In addition, although Desa and colleagues17 and Bardales and colleagues21 included suspicious cases with definite malignancies in the analysis of their data, most other authors have regarded equivocal reports as negative in the assessment of diagnostic sensitivity.

To assess further the accuracy of brush cytology in pancreatico–biliary strictures, and to assess the outcome in patients with atypical or equivocal cytological changes, we have reviewed our experience over the 6.5 year period January 1993 to June 1999.

Methods

All pancreatico–biliary brush cytology specimens submitted from the Western Infirmary, Glasgow and the Royal Infirmary, Glasgow between January 1993 and June 1999 were reviewed. Both hospitals have a major referral interest in the management of pancreatico–biliary disease and clinicians followed up their patients regularly. Four hundred and eighty nine consecutive specimens were received from 440 patients in the review period. For inclusion in the study, patients had to have a definite final benign or malignant diagnosis based either on independent histological or cytological sampling, or on clinical and radiological follow up data. The latter were obtained by case record review and by correspondence with clinicians and general practitioners. A minimum six months healthy clinical follow up period was required for confirmation of a negative cytological diagnosis.

Fifteen specimens from 15 patients (3.4%) were excluded from the study because adequate follow up data were not available (six cases), or because the patients died of uncertain or unrelated causes within six months of investigation (nine cases). Twenty specimens from 19 patients (4.3%) were considered insufficiently cellular for cytological diagnosis. Six of these patients were eventually shown to have malignant disease, nine had benign strictures, whereas the remaining four patients were lost to follow up. These unsatisfactory specimens were excluded from further assessment.

Six further patients had initial unsatisfactory specimens but subsequent sampling proved adequate for diagnosis. No significant change in the unsatisfactory rate occurred throughout the study period and there was no clear correlation between unsatisfactory sampling and the suspected tumour site. Thirty nine patients had two satisfactory specimens and one patient underwent sampling on four occasions. The study group therefore comprised 448 specimens obtained from 406 patients. There were 183 male and 223 female patients, with an age range 33–96 years (mean, 67.4). The final diagnosis was confirmed by histological and/or independent cytological assessment in 171 patients, and by clinical and radiological follow up data in 235 patients.

The specimens were obtained at ERCP by passing the brush over a guide wire placed across the stricture. The brushes were placed in normal saline or sent directly to the laboratory. Routinely, six cytospin preparations were prepared and stained according to Papanicolaou’s method. Further preparations (four to six cytospins) were examined at the discretion of the cytopathologist in problematic cases.

Most specimens were reported as definitely benign or malignant but in some an equivocal diagnosis, variably described as atypical, dysplastic, or suspicious/suggestive of malignancy, was made. Such equivocal diagnostic cases were grouped as atypical in our study.

In those patients who had two or more brush cytology specimens the more/most positive cytological diagnosis was used for clinico-pathological correlation.

Diagnostic sensitivity was calculated as true positive (TP)/TP + false negative (FN) results. Specificity was true negative (TN)/TN + false positive (FP) results. Positive predictive value (PPV) was TP/TP + FP, and negative predictive value (NPV) was TN/TN + FN results. For the purposes of analysis atypical reports were considered to be negative.

Results

Table 1 summarises the correlation between the cytological diagnoses and the final clinico-pathological diagnoses for the 406 patients.

Two hundred and fifteen patients (53%) had a negative cytological diagnosis. These specimens included clusters or regular flat sheets of uniform ductal epithelium. The cellularity
rangefromscant(onetowroups/cytopspin
preparation)tohighlycellular.Thenucleiwereroundtoovalwithonlyslightvariation(lessthan×2)insize.Inflammatorycellsand
crystallinematериалwereinonescases.Cellsreminiscentofsquamousmetaplasiawith
moderatelyenlargednuclei,densecytoplasm,andadistinctcytoplasmicmarginwerevari-
blypresent.Suchreactivechangeswere
consideredtobewithinthespectrumofneg-
vatetygology.Subsequentpathologicalorcli-
caldataconfirmedabennigoutcomein145
patientsbut70wereeventuallyshowntohave
neoplasticdisease.Ofthefalsepositivenegativecases;
40patientshadadenocarcinomaofthepan-
creas;12cholangiocarcinoma;sixampullary
neoplasms(fiveadenocarcinomasandoadenoma);twopatientseachhadcarcinoma
ofthegallbladder,hepatocellularcarcinoma,and
isletcelltumourofthepancreas;andthreepatientswerethoughttohaveabiliarystric-
tesecordarytomalignantcarcinoma.Three
patientswithfalse-negativecytologyhad
presumedpancreatico–biliarymalignancybut
theexactanatomicalsitewasnotdetermined.

Onewhundredandfiftypatients(36.9%)had
acytologicaldiagnosisofmalignancy.Thespecimenswereusuallyofmoderate tohigh
cellularity,althoughbenignelementswere
invariablypresentandusuallyaccountedfor
mostofthecellcontent.Malignantelementstypicallycomprisedlooselycohesive,crowded,
anddisorganisecellgroups,togetherwith
smallacinarclustersandsinglepleomorphic
cells.Nucleiwereneverlargerandirregular,and
nucleoliwereoftenevident.Necrosiswasan
occasionalfeature.In148cases,themalignant
specimenswerereportedasconsistentwithan
adenocarcinomaofpancreatico–biliaryorigin.
Thecytologicalappearanceswereconsidered
moresuggestiveofhepatocellularcarcinoma
inonecase,adiagnosissupportedinsitu
hybridisationforalbuminmessagerNA,22
andinasecondpatientwithknowngastric
cancerthecytologywasconsideredcon-
sistentwithmetastaticcarcinoma.

Clinicopathologicalcorrelationconfirmed
themalignantdianaesin144patients.Eight
sevenpatientshada"bio"adenocarcinoma
(includingonemixedadenocarcinoma/small
"cellurosofocrinocarcinoma),29cholangi-
ocarcinoma,eightampullaryadenocarc-
"nomafouradenocarcinomaofthegallblad-
der,onehepatocellularcarcinoma,andfive
metastaticmalignancy.Fourofthelattercases
wereconsideredconsistentwithbileduct
originonbrushcytology.However,subsequent
resectioninonepatientrevealedabiliarystric-
tesecordarytomalignantlobularcarcinoma
ofbreastratherthancholangiocarcinoma(fig
1).Thehistoryofbreastcancerwasnotavail-
ableatthetimeofcytologicaldiagnosis.Three
"urtherpatientswereclinicallysuspectedto
havebiliarycompressionasaresultofmeta-
"aticcoloniccancer,gastriccancer,and
"alignantmelanoma,respectively,buNome
hadhistologicalconfirmation.In10patients
withpositivecytologyandclinicallyconfirmed
malignantdisease,theprecise"iteoftumour
originwasnotdetermined,althoughallwerethoughttohaveprimarypancreatico–biliary
carcinoma.

Threepatientswithpositivecytologywere
foundtohavein situ neoplasia (adenomas)
involvingtheampullorthe"istocommon
bileductonpancreatico–duodenectomy(twocases)
orbiopsy(onecase)withoutevidenceof
invasive malignancy. On cytologicalreview,
these"asesshowedageneralpreservationof
architecturalarrangement,withrelativescant
"issociatedmalignantcells(fig2).However,
"ellclusterssimilartothoseseeninconfirmed
invasiveadenocarcinoma"e presentein"o
twoof"esecases.Conversely,confirmedinvasive
adenocarcinomas"europeanseriesnotun-
"omlyexhibitedanequalcytologicalpattern
tothoseoftheadenomas.These"ases
were regarded as true positive diagnoses in the
series.

There were three non-neoplastic, false posi-
tivediagnoses.Thefirstinvolveda42yearold
womanwithahistoryofprimarysclerosing
cholangitiswhodevelopedaproximallcommon
bileductstricture.Thestricturewasresected
afterthecytologicalediagnosisofcarcinomabut
histologicalexaminationrevealedonlyreactive
andinflammatorybiliaryepithelialchanges
associatedwithbiliaryandintrahepaticmicro-
calculi.Asecondbrushsampletaken"es"ix
monthspostoperativelywasconsideredhighly
atyypical,butoffiniteevidenceof
malignancy.Thepatientwasalivewithoutevidence
oftumour24months postoperatively.

Figure 1 Metastatic lobular carcinoma of breast. (A) Brush
cytology showing a small number of malignant cells
with eccentric nuclei. (B) Resection showing infiltrating
lobular carcinoma adjacent to surface epithelium (above).

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initial sample revealed three dimensional clusters of crowded gland-like groups with peripherally distributed and moulded nuclei showing a coarse chromatin pattern and distinct nucleoli (fig 3). Scattered single cells showing similar pronounced nuclear atypia were also present and there was focal cellular debris interpreted as necrosis. There were also very pronounced degenerative changes affecting both atypical and otherwise normal ductal cells.

The second false positive case was a 63 year old woman with a suspected carcinoma of the head of the pancreas. Brush cytology showed a small number of highly atypical but variably degenerate epithelial groups that were reported as consistent with an adenocarcinoma. However, no tumour was evident at laparotomy. The patient died of postoperative mesenteric ischaemia. No tumour was identified at necropsy, although histological sampling of the pancreas and biliary system was limited, and slides were not available for review.

The final false positive case involved a woman of 67 years with a periampullary stricture. Two brush cytology samples were taken, the first being considered atypical and the second reported as showing a small number of epithelial groups consistent with adenocarcinoma. The patient was not considered a suitable candidate for surgery in view of her poor general health and was therefore managed conservatively. Clinical follow up and repeat ERCP 11 months after presentation showed common bile duct stones but the stricture had resolved and there was no evidence of neoplasia. Review of the second cytology specimen revealed a small number of highly atypical but focally degenerative epithelial cells insufficient for a diagnosis of carcinoma.

Two of the false positive specimens were reported within the initial third of cases examined in this series, whereas the last was a more recent case. In retrospect, the degenerative changes evident in all cases, and the relatively scant abnormal cells in two specimens, should have led to an equivocal (atypical) rather than definite malignant diagnosis.

Brush cytology specimens from 41 patients (10.1%) were categorised as atypical. These cases exhibited a wide spectrum of cytological appearances that had been variably reported as atypical, dysplastic, or suspicious/suggestive of malignancy. Some showed a predominantly benign pattern, but with focal architectural disturbance or unusually pronounced reactive nuclear changes. At the other extreme were specimens in which cells consistent with carcinoma were present but considered insufficiently numerous or well preserved for a definite malignant diagnosis. In some cases, the presence of pronounced inflammation, evidence of calculus disease, or history of recent surgical manipulation including stenting led to an equivocal cytodiagnosis. Clinicopathological follow up data revealed that 29 patients with atypical cytological findings proved to have malignant disease whereas 12 had a benign
outcomes. The most common causes of benign atypical cytology were chronic pancreatitis and calculus disease. The proportion of atypical cases was relatively constant throughout our study period, although slightly fewer atypical cases were reported during the earliest time period.

Of the 40 patients with two or more brush specimens, 22 had a benign outcome and 18 were eventually found to have malignant disease. Ten of the patients with carcinoma had positive cytology only on a subsequent specimen, and two further patients had two atypical diagnoses; five patients with carcinoma had two negative brush samples and one patient had negative and atypical diagnoses. Of the 22 patients with benign disease, 12 had two negative cytology reports and 10 had at least one atypical diagnosis. Two of the latter patients also had false positive malignant diagnoses as described above. Overall, the later brush specimens provided a more accurate diagnosis in 16 cases, was identical to the first sample in 20 cases, and was less accurate in four cases.

On the basis of clinical, radiological, and pathological findings, of the 246 patients with established neoplastic disease 146 were considered to have pancreatic carcinoma, 48 primary bile duct neoplasia (47 cholangiocarcinomas and one adenoma), 16 primary ampullary tumours (13 adenocarcinomas and three adenomas), seven carcinoma of the gallbladder, two islet cell tumours, three hepatocellular carcinoma, and eight metastatic carcinoma. In 16 patients the precise tumour origin was not determined. There was no significant difference in the proportion of pancreatic, bile duct, ampullary, or gall bladder neoplasms identified by brush cytology in our study (87 of 146 (59.6%), 30 of 48 (62.5%), 10 of 16 (62.5%), and four of seven (57%), respectively).

One hundred and sixty patients had benign disease, most commonly biliary stones (51 cases) and chronic pancreatitis (40 cases). Twenty one patients had a variety of benign diagnoses including primary sclerosing cholangitis, duodenal diverticulum, primary parenchymal liver disease, intra-abdominal sepsis, sphincter hypertension, and benign pancreatic neoplasm (serous cystadenoma). The remaining patients with a benign outcome had no definite diagnosis, although stones and pancreatitis were suspected in many cases.

Overall, therefore, there were 147 TP diagnoses, 157 TN diagnoses, 99 FN diagnoses, and three FP diagnoses. The diagnostic sensitivity, specificity, PPV, and NPV of brush cytology for the series were 59.8%, 98.1%, 98%, and 61.3%, respectively. Most of these parameters improved over the course of the study period as summarised in Table 2. For the last 136 patients (approximately one third of the total group) the diagnostic sensitivity was 70.7%.

### Discussion

The examination of brush cytology specimens has become an established diagnostic technique in the investigation of patients with suspected pancreatic, bile duct, gallbladder, and ampullary tumours. We have reviewed 448 consecutive brush samples obtained from 406 patients and correlated the findings with pathological and clinical outcomes. To our knowledge, this is the largest series of pancreatico–biliary brush cytology specimens yet reported.

As with previous studies, we found that the brush cytology technique produced cellular samples of good quality in most instances. Only 26 of 489 (5.3%) specimens were considered inadequate for diagnosis. Seven patients with initial unsatisfactory cytology samples underwent repeat endoscopy and an adequate specimen was obtained in six cases. The number of unsatisfactory specimens has not been specifically noted in many previous studies although rates of 0–6% were documented in three series.

There was no clear correlation between unsatisfactory sampling and the site of stricture in our patients, and the proportion of cases with insufficient material was fairly constant throughout our study period.

We found that brush cytology accurately identified 147 of 246 (59.8%) neoplasms in our series, a similar result to those of most early, smaller studies reviewed by Kurzawinski and colleagues and by Foutch. Other more recent series have reported somewhat lower diagnostic sensitivities. Kocjan and Smith analysed biliary duct brushings from 131 patients in whom a histological correlation was available. The diagnostic sensitivity for patients with biopsy confirmed carcinoma was 44%, excluding dysplastic cytological diagnoses. Lee and colleagues examined brush cytology from 168 pancreatico–biliary strictures in 149 patients and found the diagnostic sensitivity to be 37%. Ponchon et al identified 45 of 127 (35%) primary bile duct carcinomas using brush cytology. Sturm and colleagues reviewed brush cytology from 294 patients with biliary strictures, including 220 patients with malignancy; 79 carcinomas (36%) were identified cytologically. Recently, Logrono et al reported 48% sensitivity for malignancy in an analysis of 183 pancreatico–biliary brush cytology specimens.

There are several possible explanations for the limited sensitivity of brush cytology in assessing pancreatic and biliary carcinomas but these can be broadly separated into sampling and interpretative errors. The former might occur when tumours at these sites show a predominantly submucosal spread, with limited or absent surface epithelial abnormality. Similarly, stricture might be caused by external compression—for example, by lymph node metastasis—without directly involving the ductal epithelium. The site of the tumour might also be important. Several studies have shown...
It is noteworthy that the diagnostic accuracy of brush cytology increased during the course of our study. In particular, the sensitivity improved from 44.3% in the initial third to 70.7% in the final third of cases. We suspect that this improvement was mainly caused by the greater experience of pathologists in interpreting pancreatico–biliary cytology specimens, but it may also have reflected better clinical sampling of malignant strictures. Our data also supported the use of repeat sampling in patients with suspected malignancy in whom initial cytology had proved negative because 10 of 18 patients with carcinoma had positive cytology only on a second brush specimen. Overall, subsequent examination proved more accurate in 16 of 40 patients undergoing two procedures, similar in 20 cases, and less accurate in only four samples. Rabinovitz et al. also showed an improved diagnostic sensitivity with repeat sampling in 65 patients with biliary strictures.20 The diagnostic sensitivity increased from 40% with one brush sample to 62% after the examination of multiple specimens.

Previous studies have shown that a diagnosis of carcinoma on brush cytology is highly reliable and many have reported 100% diagnostic specificity. There were three false positive diagnoses in our study (specificity 98.1%), principally as a result of the overinterpretation of atypical epithelial changes in patients with sclerosing cholangitis, bile duct stones, and pancreatitis. On review, it was felt that the cytological appearances in each case should have been regarded as equivocal because of the degenerative changes in all specimens and the relatively scant atypical epithelial cells in two. False positive pancreatico–biliary brush cytology diagnoses have previously occurred as a result of the misinterpretation of low grade dysplasia, reactive papillary changes with epithelial atypia, intestinal metaplasia of biliary epithelium, and the effects of previous bile duct stenting.13 18 20 27 Sturm et al. also reported two false positive cytological diagnoses among 74 patients with benign biliary strictures.12 Both patients were thought to have postsurgical bile duct stenoses and, interestingly, K-ras mutations were also identified in each case. However, neither patient had evidence of malignancy on clinical follow up. A further example of cytological overdiagnosis was described by Desa et al.,11 who recorded a case of pancreatic duct hyperplasia in which cytology had been reported as highly suspicious of carcinoma. Thus, it would appear from some recent large series that atypical but reactive epithelial changes may closely mimic malignancy in occasional pancreatico–biliary brush cytology specimens.

Three patients in our series with positive cytology proved to have adenomas involving the ampulla or distal common bile duct, but no evidence of invasive malignancy on biopsy and clinical follow up (one case) or on pancreatico–duodenectomy (two cases). Bardales and colleagues21 reported three similar cases in which duodenal or biliary brush cytology from periamphullary villous adenomas was considered consistent with carcinoma cytologically. In addition, Sawada et al1 recorded a patient with positive pancreatic duct cytology in whom resection revealed extensive “intraepithelial carcinoma” but no invasive malignancy.14 Although such cases arguably represent false positive cytological diagnoses, we do not feel that such an interpretation is justified. As with similar neoplasms in the gastrointestinal tract, adenomas involving the biliary system are considered to have malignant potential, and the operative procedures were considered appropriate in both patients undergoing resection in our series. We feel that these cases illustrate the inability of cytological assessment to distinguish reliably between in situ and invasive neoplasia in the pancreatico–biliary system, as in other sites. This is not surprising considering that histological examination is necessary to demonstrate invasion of stroma by tumour. Although the cytomorphology of the adenomatous cases we examined was characterised by a relative preservation of architectural pattern, identical appearances were seen in other specimens with confirmed invasive carcinoma. We previously described similar findings in a patient with an intraductal papillary mucinous tumour of the pancreas in which only microscopic invasive foci were seen.29 Although most patients with positive pancreatico–biliary cytology will prove to have invasive carcinoma, like Bardales and colleagues,23 we feel that it is impossible to distinguish reliably between in situ and invasive neoplasia in cytological specimens.

In our study, 41 pancreatico–biliary brush cytology specimens (10.1%) resulted in an equivocal (atypical) cytology report. There was no reduction in the proportion of atypical cases over the course of the study and, indeed, the
Brush cytology to assess pancreatico–biliary strictures

Layfield

high grade dysplasia using the criteria of have been more accurately classified as low or presented a heterogenous group, and some would prospective study, the atypical cases clearly repre-

ings in 22 of 38 brush specimens from patients made available the clinical and pathological follow up data used

assessment was not simply an e

lowest percentage was reported in the initial

investigation it could not be considered su

dysplastic cytological diagnosis merits further

thirds of patients with atypical cytological

pancreatico–biliary neoplasia.

investigation of patients with suspected

nised, brush cytology is useful in the initial

the limitations of the technique must be recog-

epithelial changes. The diagnostic sensitivity

misinterpretation of atypical but degenerative
cytological diagnoses occurred as a result of

period in our institution. Three false positive

secutive patients evaluated over a 6.5 year

therapeutic procedure.

ciently specific, in isolation, to support a radical

of pancreato–biliary malignancies but also

indefinite category, although the terminology

has varied. Layfield and colleagues provided cytological criteria for low and high grade dysplasia in addition to normal, reactive, and malignant cellular appearances. The authors recorded dysplasia in 19 of 108 (18%) pancreatic and biliary duct brush specimens. Ten of 12 patients with high grade dysplasia and three of seven with low grade dysplasia proved to have malignancy, whereas two additional patients had histologically confirmed dysplasia but no evidence of invasive carcinoma. In a subsequent series, the authors recorded that 20 of 32 patients with cytological dysplasia had clinicopathological evidence of malignancy. Using the same cytological criteria, Kocjan and Smith reported dysplasia in 10 of 131 (7.6%) bile duct brush samples; seven patients had histological evidence of malignancy whereas three had a benign outcome. Ryan and Baldauf described atypical cytological findings in 22 of 38 brush specimens from patients with pancreatico–biliary malignancies but also in two of 13 with benign disease. In our retrospective study, the atypical cases clearly represented a heterogenous group, and some would have been more accurately classified as low or high grade dysplasia using the criteria of Layfield. However, in common with previous studies, we found that approximately two thirds of patients with atypical cytological diagnoses were ultimately shown to have carcinoma. Therefore, although an atypical or dysplastic cytological diagnosis merits further investigation it could not be considered sufficiently specific, in isolation, to support a radical therapeutic procedure.

In summary, brush cytology identified 147 of 246 (59.8%) neoplasms in a series of 406 consecutive patients evaluated over a 6.5 year period in our institution. Three false positive cytological diagnoses occurred as a result of misinterpretation of atypical but degenerative epithelial changes. The diagnostic sensitivity improved during the study period. Although the limitations of the technique must be recognised, brush cytology is useful in the initial investigation of patients with suspected pancreatico–biliary neoplasia.

The authors are extremely grateful to many colleagues who made available the clinical and pathological follow up data used in this study.